REMARKS/ARGUMENTS

Claims 1-29 are pending in this application. Claim 20 has been amended to correct a typographical error. Consideration and allowance of the application is requested in view of the following comments.

Claims 1-29 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Office action, the specification fails to provide support for the limitation "rapidly disperses into granules on contact with water." Applicants respectfully that claims 1-29 are in compliance with the written description requirement as the specification includes several references to the tablets dispersing into granules on contact with water. For example:

Paragraph [0004]: In accordance with certain embodiments, the tablets rapidly disperse into granules on contact with water or body fluids. Thus, the tablets manufactured in accordance with the present invention are suitable not only for transportation in normal storage drums *(due to low friability)* for commercial distribution, but also for use in treating potassium deficiency in humans.

Paragraph [0005]: Such tablets not only rapidly disperse into granules on contact with water or body fluids, but also exhibit drug releases profile similar to that of the Hsiao tablets.

Paragraph [0007]: ...whereas the resulting tablets not only rapidly disperse upon exposure to water or body fluids, but also provide a release profile similar to that of the Hsiao tablets.

Paragraph [0009]: Tablets containing a dispersant rapidly disperse into granules upon contact with water or body fluids and exhibit an extended release profile similar to that of the Hsiao tablets.

Paragraph [0039]: Tablets containing a dispersant rapidly disperse into granules upon contact with water or body fluids and exhibit an extended release profile similar to that of the Hsiao tablets.

Paragraph [0042]: The capsule shaped monogrammed tablets (3/4" x 3/8") weighing about 2 g *(Example 11 prepared in accordance with the present invention)* exhibited a mean hardness of about 19.1 kP and a friability of 0.17% and rapidly dispersed into granules (microcapsules) on contact with water like the reference tablets, K-Dur 20 manufactured based on the disclosure of Hsiao. Furthermore, these tablets *(Example 11 prepared in accordance with the present invention)* exhibited a controlled release profile similar to that of the reference tablets, as shown in Fig. 3.

Accordingly, applicants respectfully submit that the claims currently pending comply with the written description requirement and request that the rejection be withdrawn.

Claims 1-5, 7-27 and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1 in view of Sheth et al. US 4,954,349 or Remington.

To understand to what extent the suggestions of the teachings of Gantt et al. are relevant to the rapidly dispersing tablets prepared in according to the present invention, the following two paragraphs are instructive:

Comparison of Gantt et al. vs. Present Invention:

In paragraph [0003], Applicants state that the tablets *(referring to tablets of the prior art)* failed to meet the 'industrial use' test criterion because they failed to rapidly disperse into granules on contact with water. Applicants stated again in Paragraph [0041], "Even though the tablets of Example 10 *(tablets of the prior art)* were bioequivalent to K-Dur 20, the tablets *(tablets of the prior art)* were not considered to be generically equivalent to K-Dur 20 because the tablets of Example 10 *(tablets of the prior art)* failed to disperse in water within 2 minutes as required for K-Dur® (see Physicians' Desk Reference, page 3047 of PDR Edition 57, 2003)." Gantt et al. taught the use of microencapsulated potassium chloride, compressible coating with a plasticized water-soluble polymer such as povidone, micronized silicon dioxide (Cab-O-Sil, a glidant), and microcrystalline cellulose in the tablet formulation. However, Gantt et al. could not include a disintegrant since its addition would result in poorly friable tablets that fail to sustain the drug release like the reference, K-Dur 20. In contrast, Applicants could include a disintegrant in the tablet formulation to achieve tablet dispersion/disintegration within a minute because Applicants surprisingly discovered that the compressible coating of potassium chloride microcapsules would permit the addition of a disintegrant to achieve rapid disintegration/dispersion into granules (microcapsules) while maintaining controlled release characteristics as shown below.

Applicants stated in Paragraph [0042] that the capsule shaped monogrammed tablets (3/4" x 3/8") weighing about 2 g *(Example 11 prepared in accordance with the present invention)* exhibited a mean hardness of about 19.1 kP and a friability of 0.17% and rapidly dispersed into granules (microcapsules) on contact with water like the reference tablets, K-Dur 20 manufactured based on the disclosure of Hsiao. Furthermore, these tablets *(Example 11 prepared in accordance with the present invention)* exhibited a controlled release profile similar to that of the reference tablets, as shown in Fig. 3.

RECEIVED
CENTRAL FAX CENTER
MAY 14 2007

Multifunctional Excipients:

Many excipients have dual or even multiple functions; typically, a given excipient will have a primary function and one or more additional functions wherein it is less effective. For example, microcrystalline cellulose primarily enhances the compaction properties of a formulation. However, when present at high concentrations in tablet formulations, it acts as a disintegrant. Pharmaceutical reference books such as Remington: The Science and Practice of Pharmacy, Handbook of Pharmaceutical Excipients published by the Pharmaceutical Press (Publication Division of the Royal Pharmaceutical Society of Great Britton) and the American Pharmaceutical Association, etc define 'lubricants', 'Glidants', 'Disintegrants' etc. For example, commonly used lubricants include talc, magnesium stearate, calcium stearate, stearic acid, hydrogenated vegetable oils and polyethylene glycols (see Remington, 19th Edition, Chapter 92, page 1618). The concentrations of different lubricants, order of mixing, etc. are disclosed. To overcome the waterproofing characteristics of the most widely used magnesium stearate, sodium lauryl sulfate is sometimes included, states Remington. Nowhere does Remington list silicon dioxide to be used as a lubricant. In fact, Remington defines a glidant and states that colloidal silicon dioxide (Cab-O-Sil) is the most commonly used glidant. Remington also states that talc also is used and may serve the dual purpose as lubricant/glidant. Handbook of Pharmaceutical Excipients, Fourth Edition, states on page 161 lists Cab-O-Sil as an absorbent, emulsion stabilizer, glidant, suspending agent, tablet disintegrant (see Functional Category). Again there is no mention of colloidal silicon dioxide being used as a lubricant.

Sheth et al. included colloidal silicon dioxide in the list of lubricants. Sheth et al. disclosed the use of a mixture of talc and magnesium stearate as a lubricant in all the tablet formulations while colloidal silicon dioxide was used only in the polymer (ethycellulose) coating solution. This is surprising since presuming that Sheth et al. believed that silicon dioxide are equivalent in their function as a lubricant, why would one use only the mixture of talc and magnesium stearate and not a mixture of colloidal silicon dioxide and talc or magnesium stearate. Magnesium stearate, talc or silicon dioxide is typically suspended in a polymer coating formulations in organic solvent mixtures that are sprayed onto small inert particles in fluid bed equipment in order to eliminate/ minimize static charge build-up due to fluidization. Sheth et al. failed to demonstrate rapid disintegration/dispersion into granules on contact with water and/or drug release profiles similar to that of the tablets prepared in accordance with the present

invention. Hence it is difficult to imagine a skilled person would be tempted to follow Sheth et al. to formulate controlled release formulations of potassium chloride.

Furthermore, as discussed in the background of the present application, tablets prepared in accordance with a prior art (Gantt et al.) containing compressible coated potassium chloride microcapsules, microcrystalline cellulose, and magnesium srearate as a lubricant failed to rapidly disperse/disintegrate into granules on contact with water. When a disintegrant was incorporated into the tablet composition to promote rapid disintegration in accordance with the teachings of Remington (see Examples 1-3), tablets weighing about 2 g exhibited a hardness of less than 5 kP and unacceptable friability. When tablets from the compression blend containing compressible coated potassium chloride microcapsules, and microcrystalline cellulose without including magnesium stearate were compressed into scored tablets weighing about 2 g, the tablets exhibited poor friability (greater than 1% loss, see Examples 4, 5, and 9). These tablets also failed to meet the disintegration time specification set out in the present application.

The Office action indicates that "the burden has shifted to applicant to show that the compressed tablet of Gantt does not exhibit the claimed properties, because Gantt uses the same ingredients and the same method using the same parameter for the same active." Applicants respectfully submit that such data is present in the application as discussed above. Furthermore, Examiners must consider comparative data in the specification which is intended to illustrate the claimed invention in reaching a conclusion with regard to the obviousness of the claims. *In re Margolis*, 785 F.2d 1029, 228 USPQ 940 (Fed. Cir. 1986).

Applicants respectfully submit that this clearly shows that Gantt not only fails to disclose the present invention but also that the present invention is novel and non-obvious over Gantt. As discussed above, magnesium stearate and silicon dioxide although described as being equivalent in certain pieces of prior art do not function as equivalent components in the composition set forth in the present application. Therefore, unexpected benefit is evidence of the non-obviousness of the invention. Therefore, applicants respectfully request that the rejection be withdrawn.

Claims 6 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1, in view of Sheth et al. US 4,954,349 or Remington, and Oshlack et al. US 5,472,712. Gantt et al. and/or Oslack et al. do not disclose or suggest the use of diethyl phthalate or anoher plasticizer for imparting compressible coating on microcapsules which when incorporated into the tablet together with a

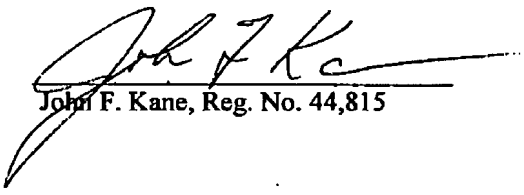
disintegrant and colloidal silicon dioxide would result in tablets that rapidly disperse/disintegrate on contact with water.

Applicants respectfully disagree with the Office's contention that using silicon dioxide as a lubricant is well known in pharmaceutical art for reasons elaborated earlier. The Office action refers to claims 11 and 20 of Gilinski US 2006/0222699 who teaches the art of making HPMC capsule parts, body and caps, by dipping hot molds and pins into the HPMC solution in which silicon dioxide is dispersed and subjecting to a drying process. Whether silicon dioxide is used as a lubricant or as a glidant in this application has nothing to do with its use in the tablet formulation. Applicants demonstrated that the use of magnesium stearate, the widely used lubricant, results in tablets of the present application with unacceptably poor hardness and friability. Chiodini et al. claim the use of colloidal silicon dioxide as a lubricant without providing any evidence for its effectiveness as a lubricant.

Applicants further submit that the claims of the pending application are novel and non-obvious with the cited references which fail to disclose or suggest a process set forth in the claims of the pending application which provide a tablet that rapidly disperses into granules on contact with water. Furthermore, for at least this reason as well, applicants submit that the claims of the pending application are novel and non-obvious over the cited art.

Therefore, applicants submit that the claims are in condition for allowance and request that the timely notice of allowance be issued in this case. If the Examiner wishes to discuss any aspect of this response, please contact the undersigned at the telephone number indicated below.

Respectfully submitted,



John F. Kane, Reg. No. 44,815

THOMPSON HINE LLP
2000 Courthouse Plaza NE
10 West Second Street
Dayton, Ohio 45402-1758
(937) 443-6816

480130-v1